

REMARKSI. Claims under Consideration

Claims 1-24 are currently pending in this application. Further to a restriction requirement, claims 5-17 have been withdrawn from consideration as directed to a non-elected invention. Claims 1-4 and 18-24, which are directed to a fusion protein, have been examined on the merits and rejected under 35 U.S.C. § 112, first paragraph as lacking both written description and enablement.

II. Supplemental Oath

The Office asserts that the claims, as amended in applicants' reply filed November 7, 2002, "no longer substantially embrace the invention as set forth in the statement of invention and/or the original claims." Accordingly, the Office states that "applicant is required to file a supplemental oath or declaration." For the following reasons, applicants respectively disagree with this requirement.

As an initial matter, applicants note that the Office fails to explain what it considers to be the newly claimed subject matter. In particular, the Office has not identified the differences between the original statement of the invention and the subject matter as claimed in applicants' November 7, 2002 reply. Rather, the Office summarily concludes

that the claimed invention is not “substantially embraced” by the original disclosure. For this reason alone, the requirement is incomplete and improper.

Moreover, applicants submit that the Office’s conclusion is in error. Claim 1, as amended in applicants’ November 7, 2002 reply, reads:

1. (Amended) A fusion protein comprising (a) a first domain to which a ligand binds that comprises a steroid hormone receptor, (b) a second domain that (i) comprises a steroid hormone receptor and (ii) associates when a ligand binds to the first domain, and (c) a third domain comprising a cytokine receptor or a part thereof that imparts proliferation activity to a cell upon the association of the second domain.

Applicants’ specification clearly embraces the claimed subject matter. The specification, for example, under the heading “Disclosure of the Invention,” specifically states, at page 4 (lines 3-7), that

[t]he present invention relates to a fusion protein comprising a ligand-binding domain, a domain that associates when a ligand binds to the ligand-binding domain, and a domain that imparts proliferation activity to a cell upon the association.

Similarly, claim 1, as filed, is directed to

a fusion protein comprising (a) a ligand binding domain, (b) a domain that associates when the ligand binds to the domain of (a), and (c) a domain that imparts proliferation activity to the cells upon the association.

Claim 2, as filed, is directed to

The fusion protein of Claim 1, wherein the “ligand-binding domain” is derived from a steroid hormone receptor.

And applicants' specification, for example, at page 4 (lines 16-17), states:

a domain comprising; a cytokine receptor or a part thereof that imparts proliferation activity to a cell...

Claim 1, as amended in applicants' November 2, 2002 reply, therefore, merely incorporates the limitations of claim 2, and cannot be construed as no longer substantially embracing the invention set forth in the statement of the invention or in the original claims. Claim 1 merely includes a specific embodiment of the invention previously described and claimed, namely an embodiment wherein domains (a) and (b) comprise a steroid hormone receptor and domain (c) comprises a cytokine receptor. This embodiment is not only substantially embraced by original claim 1 but specifically covered by original claim 2. Furthermore, this claimed embodiment is specifically identified within the original specification as a preferred embodiment. See, for example, page 6 (lines 2-4) ("Any ligand can be used but a steroid hormone is preferable") and page 6 (lines 7-9) ("Any cytokine receptor can also be used"). Finally, these claims reflect the specific examples set forth in the specification. Thus, it is unclear how the Office has concluded that the instant claims are not "substantially embraced" by the statement of the invention and/or the original claims.

In view of the above, Applicants respectfully submit that the Office's requirement is in error and should be withdrawn.

III. Rejections Under 35 U.S.C. § 112, First Paragraph

Written Description

The Office has asserted that claims 1-4 and 18-24 are unpatentable under the first paragraph of 35 U.S.C. § 112 because the applicants have failed to provide the requisite written description of the claimed subject matter. In particular, the Office asserts that Applicants' disclosure is "insufficient to support the position ... that applicant possessed the entire genus being claimed." Applicants respectfully disagree.

The statutory language of 35 U.S.C. § 112, first paragraph, in issue stipulates that

the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same ...

The legal standard for sufficiency of a patent application's written description is whether that description "... reasonably conveys to the artisan that the inventor had possession at that time of the ... claimed subject matter." *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (quoting *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983))); *Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993) (citation omitted).

Claim 1, as amended, reads:

A fusion protein comprising (a) a first polypeptide and (b) a second polypeptide, wherein said first polypeptide comprises a ligand binding domain of a steroid hormone receptor that, upon ligand binding, self-associates, and wherein said second

polypeptide comprises a cytokine receptor or a proliferation-inducing part thereof that, upon said self-association of said first polypeptide, imparts proliferation activity to a cell.

Applicants' specification conveys, with reasonable clarity to the skilled persons, that the inventors possessed the presently claimed invention. First, applicants' specification unmistakably informs the skilled person of the claimed fusion protein that includes both a steroid hormone receptor polypeptide and a cytokine receptor polypeptide. For example, as filed, the specification at page 3 (lines 20-25) states:

[T]he present inventors have thought of constructing a chimeric gene between the G-CSF receptor gene and the estrogen receptor gene, introducing the chimeric gene into cells, and externally stimulating the cells by estrogen to forcibly dimerize the G-CSF receptor portion of the chimeric gene product [a fusion protein].

Next, the specification at page 4 (lines 3-6), in describing the requisite domains of the fusion protein, states:

The present invention relates to a fusion protein comprising a ligand-binding domain, a domain that associates when a ligand binds to the ligand-binding domain, and a domain that imparts proliferation activity to a cell upon association.

Further, with respect to a ligand binding domain of the fusion protein, which further includes a self association domain, the specification at page 6 (lines 2-7) states:

Any ligand can be used in the present invention as long as it acts on a specific protein to cause association of the protein, but a steroid hormone is preferable. Examples of the steroid hormone include estrogens, androgens, progesterone, glucocorticoids, and mineral corticoids. They are used in combination with their respective receptor proteins.

While with respect to the cytokine receptor portion of the fusion protein, the specification, at page 6 (lines 7-12) states:

Any cytokine receptor can also be used in the present invention as long as it imparts proliferation activity to a cell upon association. Examples of the cytokine receptor are those belonging to the cytokine receptor family including G-CSF and those belonging to the tyrosine receptor family including c-kit and flk2/flt3.

And with respect to the proliferation-inducing domain of the cytokine receptor, the specification at page 6 (lines 13-18) states:

As the "domain which imparts proliferation activity to a cell" of the fusion protein according to the present invention, it is possible to use a molecule that transmits the intracellular proliferation signal, for example, an entire molecule of a cytokine receptor. It is also possible to use only a domain in the molecule that imparts proliferating activity to a cell.

Given these passages of applicants' specification alone, there can be no doubt that applicants have satisfied the written description requirement, and that applicants have unambiguously described their invention so as to reasonably convey to persons skilled in the art that the inventors possessed the subject matter in question.

In addition to the aforementioned description, applicants' specification, as filed, further describes several different steroid hormone receptor:cytokine receptor fusion proteins. Exemplary fusion proteins are described in Figure 1, and at page 7 (line 22) – page 8 (line 2) which states:

Fig. 1 (A) shows a chimeric molecule between the G-CSF receptor and the estrogen receptor (GCRER). (B) shows a mutant of the chimeric molecule between the G-CSF receptor

and the estrogen receptor, deficient in the 5th through 195th amino acids of the G-CSF receptor (GCR (Δ 5-195)/ER). (C) shows a mutant of the chimeric molecule between the G-CSF receptor and the estrogen receptor, deficient in the 5th through 195th amino acids and the 725th through 756th amino acids of the G-CSF receptor (GCR (Δ 5-195, 725-756)/ER).

Furthermore, applicants note that their specification, for example, at page 9 (lines 12-24) describes exemplary methods for engineering nucleic acid molecules to generate sequences that express the presently claimed fusion proteins. In particular, the specification states:

In order to produce a chimeric protein comprising the entire G-CSF receptor and the ligand (estrogen)-binding domain of the estrogen receptor (hereafter designated simply as "GCRER"), the fusion gene having cDNAs that encode the respective proteins (Fig. 1(A)) was constructed. Next, a mutant of the fusion gene, "GCRER," which is deficient in the 5th residue, Glu, through the 195th residue, Leu, of the G-CSF receptor extracellular domain (hereafter designated simply as "GCR Δ (5-195)/ER") was constructed, in order to produce a chimeric protein that lacks reactivity against G-CSF (Fig. 1(B)). Further, a mutant was constructed by deleting a portion containing the differentiation-inducing domain (725-756) of the G-CSF receptor from the mutant (hereafter designated simply as "GCR Δ (5-195, 725-756)/ER") (Fig. 1(C)).

In addition, the written description rejection is without merit as it relates to dependent claims 2-4 and 18-24. For example, claim 2 limits the second domain to the G-CSF receptor and claim 4 limits the first domain to the estrogen receptor. Furthermore, claims 18-24 are directed to working examples explicitly described in applicants' specification. Moreover, as the genus recited in claims 2-4 and 18-24 is significantly less variable, the working examples disclosed are sufficiently representative.

Evidence in the scientific literature also plainly further supports applicants' position that the disclosed exemplary estrogen and G-CSF receptors are representative of steroid hormone and cytokine receptors respectively. For example, applicants' exemplary estrogen receptor is representative of steroid hormone receptors. As evidence of this assertion, applicants direct the Office's attention to Thornton ("Evolution of vertebrate steroid receptors from an ancestral estrogen receptor by ligand exploitation and serial genome expansions." *Proc. Natl. Acad. Sci. U.S.A.* 98:5671-5676, 2001; copy enclosed). As is evident from the title, steroid receptors evolved from an ancestral estrogen receptor, and given this evolutionary connection, biological similarities are known to exist in this conserved receptor family.

In addition, applicants' exemplary G-CSF receptor is representative of cytokine receptors. Indeed, no substantial variation exists, with respect to a proliferation-inducing domain, within the family of cytokine receptors. First, the cytoplasmic region of the G-CSF receptor is known in the art to have a membrane-proximal domain, which has two conserved subdomains designated box 1 and box 2. The membrane-proximal domain is known to be a binding site for the Jak family of tyrosine kinases and is essential for mitogenic signaling (see, for example, page 381, col. 2, Omura et al. ("Acceleration of granulocyte colony-stimulating factor-induced neutrophilic nuclear lobulation by overexpression of Lyn tyrosine kinase." *Eur. J. Biochem.* 269: 381-389, 2002)).

Furthermore, the membrane-proximal domain that includes the box1/box2 motif is well conserved among cytokine receptor family members. As evidence of this assertion, applicants direct the Office's attention to Ihle, ("Cytokine receptor signaling." *Nature*, 377:591-594, 1995; copy enclosed) and Murakami et al. ("Critical cytoplasmic region of the interleukin 6 signal transducer gp 130 is conserved in the cytokine receptor family." *Proc. Natl. Acad. Sci. USA*, 88:11349-11353, 1991; copy enclosed). In particular, applicants direct the Office's attention to Figure 2 and Figure 1B of Ihle and Murakami, respectively.

In addition to the G-CSF receptor, it has been shown that this membrane-proximal region comprising box1/box 2 is vital for cell proliferation signal transduction in a variety of cytokine receptors such as IL-6R (gp 130) and IL-2R (see, Murakami et al.) and the EPO receptor (see Ihle, for example, Fig. 1). Therefore, as there is no substantial variation among cytokine receptors with regard to the domain required for transducing the proliferation signal, applicants description and examples utilizing the G-CSF receptor are plainly representative of cytokine receptors.

Furthermore, as cytokine receptors were well studied, at the time of filing the instant application, a skilled artisan could routinely isolate a proliferation-inducing domain of a cytokine receptor without undue experimentation.

Applicants further note that cytokine receptors, like the G-CSF receptor, share additional characteristics recognizable by one skilled in the art. For example, cytokine

receptors, like the G-CSF receptor, dimerize when activated. Indeed, as noted by Heldin, ("Dimerization of cell surface receptors in signal transduction." Cell 80:213-223, 1995; copy enclosed), at page 213, col. 1, "Growth factors and cytokines exert their effects via binding to cell surface receptors...such receptors often are activated by ligand-induced dimerization or oligomerization." (see Heldin et al., Abstract Lines 5 to 8) . In addition, Alexander et al. ("Point mutations within a dimer interface homology domain of c-Mpl induce constitutive receptor activity and tumorigenicity." The EMBO Journal 14:5569-5578, 1995; copy enclosed) at page 5569, abstract, describe that "[a] recurring mechanism for the activation of haemopoietin receptors is the formation of functional complexes by receptor subunit oligomerization."

Applicants also point out that the G-CSF receptor belongs to the Class I cytokine receptor family, which is the largest of the two cytokine receptor families (see, for example, Heldin et al., Table 1, page 214). The structural features of the Class I cytokine receptor family, known when applicants filed their application, are disclosed in detail on page 216, under "Cytokine receptors."

In sum, applicants' specification plainly meets the written description standard by providing not only clear language describing the claimed fusion proteins, but also by describing several working examples of fusion proteins. This description, which is beyond dispute, would be recognized by one skilled in the art. Moreover, applicants have, from the time they originally filed this application, claimed this type of fusion protein as part of their

invention. One skilled in the art therefore certainly would recognize that, at the time of filing, the inventors were in possession of such claimed fusion proteins. The written description requirement of § 112, first paragraph has been satisfied by applicants, and the rejection of claims 1-4 and 18-24, as amended, should be withdrawn.

For the record, applicants further note that it appears to be the Office's position that applicants have not disclosed a suitable number of fusion genes falling within the scope of the claim to support the language in the claims. The Office relies on *In re Shokal*, 113 USPQ 283 (CCPA 1957) to support its position. In particular, the Office relies on *Shokal* for the following proposition:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. 1309, 97 F.2d 623, 38 USPQ 189 In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of a small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary.

* * *

We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

The Office, in essence, takes the position that in order to support the broad generic language found in applicants' claim, applicants' specification must be equally broad in naming, and in use in examples, of representative species encompassed by the claim language. The Office's reliance on *Shokal* in this situation is misplaced.

Given that applicants' specification, as is discussed above, not only describes, in clear language, the presently claimed invention but also describes, in detail, numerous species encompassed by the amended claims, the citation to *Shokal* is not applicable to this case. Unlike applicants' specification in this application, appellant's generic claim in *Shokal* was not disclosed in its specification in clear language, and appellant therefore relied on exemplary species, recited in its specification, to both illustrate and define the claimed genus. Applicants also note that "[m]ention of representative compounds encompassed by generic claim language clearly is not required by §112 or any other provision of the statute." *In re Robins*, 429 F.2d 452, 456 (C.C.P.A. 1970). Moreover, "a specification may, within the meaning of 35 U.S.C. § 112, contain a written description of a broadly claimed invention without describing all species that claim encompasses." *Utter v. Hiraga* 845 F.2d 993, 998 (Fed. Cir. 1988). Applicants' specification clearly conveys to the skilled person that applicants had possession of the claimed subject matter, the written description requirement of § 112 is therefore satisfied and the rejection should be withdrawn.

Enablement

The Office has also asserted that claims 1-4 and 18-24 are unpatentable under the first paragraph of 35 U.S.C. § 112 because the applicants have failed to comply with the enablement requirement. Applicants respectfully disagree.

The Office first asserts that applicants' specification has not taught the skilled persons how to use the claimed fusion protein. Contrary to this assertion, applicants' specification clearly teaches the skilled persons how to use the claimed gene products. Applicants' specification makes clear that, to selectively proliferate a cell, a gene encoding a fusion protein is engineered, introduced into a cell, expressed in the cell, and the cell is then stimulated with a ligand that induces cell proliferation. As noted above, applicants' specification, for example, at page 3 (line 20) – page 4 (line 2) states:

[T]he present inventors have thought of constructing a chimeric gene between the G-CSF receptor gene and the estrogen receptor gene, introducing the chimeric gene into cells, and externally stimulating the cells by estrogen to forcibly dimerize the G-CSF receptor portion of the chimeric gene product [a fusion protein].

Thus, the present invention was completed by developing a new system for selectively amplifying hematopoietic stem cells into which a gene has been introduced by activating the G-CSF receptor portion of the chimeric gene product [a fusion protein] through external stimulation with estrogen...

Applicants' specification also, as noted above, provides clear working examples of applicants' claimed invention. Finally, under the heading of "Industrial Applicability," found at page 15, applicants provide still additional information on how to use the

claimed fusion proteins, which are expressed from an exogenous gene. Given these aforementioned passages, there can be no dispute that applicants' specification teaches artisans how to use the claimed product.

The Office further contends that applicants' specification "does not reasonably suggest that applicant possessed the [claimed] genus of fusion proteins..." Applicants again respectfully disagree.

Applicants' claimed invention, as noted above, is described in clear language in their specification. Applicants' specification, as also noted above, at page 6, expressly describes several steroid hormone receptors useful in engineering the claimed fusion protein, such as receptors of androgens, progesterone, glucocorticoids, and mineral corticoids. Applicants further describe, as noted above, exemplary cytokine receptors as those belonging to the cytokine receptor family that include G-CSF and those belonging to the tyrosine receptor family including c-kit and flk2/flt3. Several fusion protein examples are described in the specification and clearly support the claimed genus (see, for example, Examples 1-6). Finally, as also described above, applicants note that their disclosed exemplary estrogen and G-CSF receptors are representative of steroid hormone and cytokine receptors respectively. Clearly, based on applicants' description, one skilled in the art would recognize that applicants' claimed fusion protein invention encompassed a variety of steroid and cytokine receptors, not limited to the specific examples described by applicants. Moreover, there can be no doubt that applicants'

specification conveys that the inventors possessed the claimed genus of fusion proteins.

The Office has also asserted that the “specification is silent as to how one would ensure that the proteins of the various domains would retain activity and not be toxic to the host cells.” This concern is unwarranted. There is simply no reason to expect the claimed fusion proteins to be inactive or toxic, particularly in light of the successes documented in the examples. For instance, as discussed in Examples 2 and 6, none of the cells transfected with the various chimeric GCRER plasmids (i.e., cells producing various GCRER fusion proteins) suffered any negative consequences. Furthermore, those skilled in the art routinely screen many fusion proteins in order to isolate a fusion protein having the desired effect; such screening is routine in the art and does not constitute undue experimentation.

The Office also states “the specification does not teach that any fusion protein was produced from such constructs, nor shown to have any activity.” This statement is fundamentally wrong. In Example 2, Applicants describe the transfection of Ba/F3 cells with a number of GCRER constructs. Applicants’ specification, in Example 2, at page 11 (lines 3-5) makes perfectly clear that fusion proteins were clearly identified:

The production of the desired fusion protein in the cells was confirmed by western blotting.

Similarly, in Example 5, Applicants describe the transfection of bone marrow cells with similar GCRER constructs. As a result of such transfections, these cells then produced fusion proteins commensurate with the pending claims. Accordingly, the description of fusion proteins is inherent from the description of transfection and subsequent culturing. Furthermore, the fusion proteins were not only confirmed to be expressed but were confirmed to be active. Specifically, all the transfected cells demonstrated estrogen-dependent proliferation, confirming that the activity of fusion protein domains was not affected. Thus, the specification does indeed teach that functional, active fusion proteins were produced from the disclosed constructs.

Furthermore, applicants note that the test of enablement is whether one reasonably skilled in the art could make and use the claimed invention (here, fusion proteins) from the disclosure in the patent coupled with information known in the art without undue experimentation. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. As the Office correctly notes, there are many factors to be considered when determining whether the specification is enabled and whether any necessary experimentation is "undue". These factors include: the breadth of the claims; the nature of the invention; the state of the prior art; the level of ordinary skill in the art; the level of predictability in the art; the amount of direction provided by the

inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention.

In this case, given the state of the prior art and the level of ordinary skill, the production of a fusion protein from a gene construct is routine and straightforward. Thus, a fusion gene implicitly and inherently describes and enables its corresponding fusion protein. Any degree of unpredictability is counterbalanced by the fact that the present specification not only provides a high level of explicit direction as to how to make and use fusion proteins within the scope of the claims from the exemplary fusion genes but also provides numerous working examples of fusion genes and their corresponding fusion proteins.

Applicants also note that a specification is presumed to be in compliance with the enablement requirement of 112, first paragraph. The burden is on the Patent Office to establish a reasonable basis to question enablement. In this case, the Office has not met its burden and provides neither scientific reasoning nor evidence to support this ground of the rejection.

Finally, the Office contends that “[t]he specification has not set forth a reproducible procedure whereby such deletion mutants are used in any method, much less a method that satisfies the utility requirement of 35 U.S.C. § 101.” Applicants also respectfully disagree with this assertion.

First, as is explained above, applicants’ specification not only provides ample

description of the methods for making and using the claimed fusion proteins, but in fact demonstrates actual reduction to practice several times. The Office's attention is again directed to Examples 1 and 4, which provide straightforward working examples which describe the construction of three selective amplification fusion genes of the present invention - GCRER, GCRA(5-195)/ER, GCRA(5-195, 725-726)/ER, alone and ligated with IRES-CD24. Applicants submit that these examples are sufficiently detailed to allow one of ordinary skill in the art to reproduce the invention, absent undue experimentation.

Second, to be properly rejected under § 101, the Revised Interim Utility Guidelines Training Materials Guidelines set forth that a case must represent one of those rare instances that meets the stringent criterion of being "totally incapable of achieving a useful result," *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555 (Fed. Cir. 1992), as cited in the Legal Analysis accompanying the Utility Examination Guidelines (M.P.E.P. § 2107.01-II). The only instances in which the federal courts have found a lack of patentable utility were where, "based upon the factual record of the case, it was clear that the invention could and did not work as the inventor claimed it did" (M.P.E.P. § 2107.01-II, emphasis added). These rare cases have been ones in which the applicant either (a) failed to disclose any utility for the invention, or (b) asserted a utility that could be true only "if it violated scientific principle, such as the second law of thermodynamics, or a law of nature, or was wholly inconsistent with contemporary knowledge in the art" (M.P.E.P. § 2107.02-IIIB).

Procedurally, the M.P.E.P. makes clear that the burden is on the Office to provide a detailed, reasoned explanation for the rejection that is supported, if possible, by documentary evidence indicating why the asserted utility is more likely than not "incredible." "An applicant's assertion of utility creates a presumption of utility" (M.P.E.P. § 2107.01-III(A)); "Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being 'wrong,' even when there may be reason to believe that the assertion is not entirely accurate" (M.P.E.P. § 2107.01-III(B)). Conversely, if the Office determines that the claimed invention has a credible utility, neither a 35 U.S.C. § 101 nor a related 35 U.S.C. § 112 rejection may be applied (or, upon rebuttal of the Office's position, both rejections must be simultaneously reversed).

In the present case, applicants assert a clear utility in the specification for the claimed fusion proteins, that are, on their face, credible. Applicants again assert, as noted in their specification, that the present invention provides fusion proteins that can be used to proliferate cells. Additionally, applicants note that one skilled in their art would readily appreciate the utility of applicants' claimed invention. No evidence has been made of record to dispute the utility of applicants' invention, and on this basis this ground of the rejection should also be withdrawn.

CONCLUSION

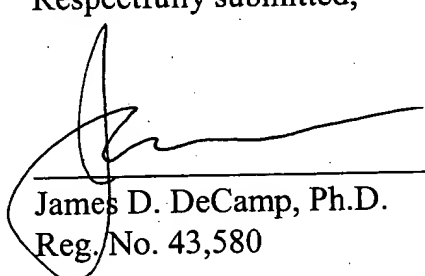
Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the final Office action for three months, to and including March 16, 2004, and a check for \$475.00 in payment of the required extension fee. Applicants also enclose a Notice of Appeal, along with the requisite fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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James D. DeCamp, Ph.D.
Reg. No. 43,580

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045